

AMERICAN HOME PROD CORP
 1998.12.09 1998-208540(+1998US-208540) (2000.06.15) C07D
 405/12, A61K 31/63, A61P 31/12, C07D 417/12, 213/75, 213/81
 Novel thiourea derivatives useful for treating diseases associated
 with herpes viruses (Eng)
 C2000-128176 N(AE AL AM AT AU AZ BA BB BG BR BY CA CH
 CN CR CU CZ DE DK DM EE ES FI GB GD GE GH
 GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
 LR LS LT LU LV MA MD MG MK MN MW MX NO
 NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
 TZ UA UG UZ VN YU ZA ZW) (A/T BE CH CY DE
 DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC
 MW NL OA PT SD SE SL SZ TZ UG ZW)

Addl. Data: BLOOM J D, DIGRANDI M J, DUSHIN R G, LANG S A,
 O'HARA B M
 1999.12.06 1999WO-US28892

NOVELTY

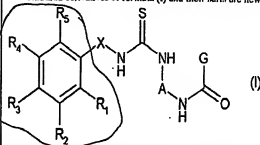
Thiourea derivatives (I) are new.

reactant II

DETAILED DESCRIPTION

(10-1, 1-1, 14-1A, 1-1)

Thiourea derivatives of formula (I) and their salts are new.



$R_1, R_2 = H$, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C perhaloalkyl,
 3-10C cycloalkyl, 3-10C heterocycloalkyl, aryl, heteroaryl,
 halo, CN , NO_2 , CO_2R_6 , COR_6 , OR_6 , SR_6 , SOR_6 , SO_2R_6 ,
 $CONR_7R_8$, NR_7NR_8 , NR_7R_8 or $W-Y-(CH_2)_n-Z$; or
 R_1+R_2 or $R_3+R_4 = 3-7$ membered heterocycloalkyl or heteroaryl;
 $R_6, R_7 = H$, 1-6C alkyl, 1-6C perhaloalkyl or aryl;
 $R_8 = H$, 1-6C alkyl, 1-6C perhaloalkyl, 3-10C cycloalkyl, 3-10C
 [WO 200034269-A+]

heterocycloalkyl, aryl or heteroaryl; or

$R_1+R_2 = 3-7$ membered heterocycloalkyl;

A = heteroaryl;

W = O, NR_6 or is absent;

Y = CO or CO_2 or is absent;

Z = 1-4C alkyl, CN , CO_2R_6 , COR_6 , $CONR_7R_8$, $OCOR_6$, NR_7COR_6 ,
 $OCOR_6$, OR_6 , SR_6 , SOR_6 , SO_2R_6 , $SR_6NR_7R_8$ (sic), NR_7R_8 or
 phenyl;

G = aryl or heteroaryl;

X = bond, NH, 1-6C alkyl, 2-6C alkenyl, 1-6C alkoxy, 1-6C thioalkyl,
 1-6C alkylamino or CH₂;

J = 1-6C alkyl, 3-7C cycloalkyl, phenyl or benzyl; and
 n = 1-6.

ACTIVITY

Virucide. In a V2V antiviral (ELISA) assay N-[2-(5-chloro-2,4-
 dimethoxy-phenyl)-thioureido]-pyridin-3-yl]-2-fluorobenzamide
 inhibited viral replication by 90% at a concentration of 10 micro g/ml.

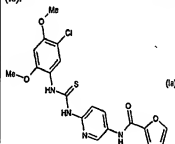
USE

(I) are useful for inhibiting the replication of a herpes virus and
 treating herpes virus infections such as human cytomegalovirus,

herpes simplex virus, and varicella zoster virus (claimed), (I) are also
 useful for inhibiting and/or treating diseases associated with herpes
 viruses including Epstein-Barr virus, human herpes viruses-6 and -7,
 and Kaposi herpes virus.

SPECIFIC COMPOUNDS

31 Compounds (I) are claimed e.g. furan 2-carboxylic acid [6-[3-
 (5-chloro-2,4-dimethoxy-phenyl)-thioureido]-pyridin-3-yl]-amide
 (Ia).



[WO 200034269-A+]

2000-423357/36

ADMINISTRATION

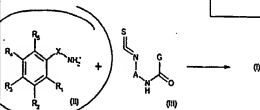
Dosage is 0.01-1000 mg/kg/day orally or 0.1-100 mg/kg/kg/day
 parenterally.

EXAMPLE

To a solution of 2,5-dichloroaniline (0.16 g) in THF (20 ml) was
 added freshly prepared 1,1'-thiocarbonyldiimidazole (0.2 g) and the
 mixture was stirred for 30 minutes at room temperature. [1,2,3]-
 Thiadiazole-4-carboxylic acid (4-amino-phenyl) amide (0.22 g) was
 added and the mixture was stirred for 6 hours. Work up gave [1,2,3]-
 thiadiazole-4-carboxylic acid [4-[3-(2,5-dichlorophenyl)-thioureido]-
 phenyl]-amide.

TECHNOLOGY FOCUS

Organic Chemistry - Preparation: (I) can be prepared by reacting
 appropriately substituted amines of formula (II) with appropriately
 substituted isothiocyanates of formula (III).



(162pp) 1894DwgNo.007

[WO 200034269-A/2]

BEST AVAILABLE COPY

(C) 2004 Copyright Derwent Information Ltd.